

Express Mail No. EL 739387695 US

JMA 2977

PATENT

What is claimed is:

1. A composition comprising:

(a) one or more materials selected from the group consisting of fibroblast growth factors, vascular endothelial growth factors, endothelial cell growth factors, transforming growth factors, chitosan, bone, platelet derived endothelial growth factors, placental growth factors, angiogenin, interleukin-8, granulocyte colony-stimulating growth factor, and supernatant fluid from a culture of cells known to produce angiogenic factors;

(b) a material comprising demineralized bone matrix, non-decalcified bone matrix, with or without hyaluronic acid;

(c) a scaffolding material selected from the group consisting of cancellous bone, chitosan, chitosan-protein, and chitin-protein fibers; and

(d) a gel material selected from the group consisting of chitosan, imidazolyl chitosan, methylpyrrolidinone chitosan, carbodiimide chitosan, glutaraldehyde chitosan, a mixture of alginate with chitosan or a chitosan derivative, alginate, hyaluronic acid, or a mixture of hyaluronic acid with chitosan or chitosan derivative.

2. A composition comprising:

(a) one or more angiogenesis-stimulating materials;

(b) one or more osteoinductive materials;

(c) one or more scaffolding materials; and

(d) one or more gel materials.

Express Mail No. EL 739387695 US
JMA 2977
PATENT

3. A composition comprising:

(a) one or more angiogenesis-stimulating materials selected from the group consisting of fibroblast growth factors, vascular endothelial growth factors, endothelial cell growth factors, transforming growth factors, chitosan, bone, platelet derived endothelial growth factors, placental growth factors, angiogenin, interleukin-8, and granulocyte colony-stimulating growth factor;

(b) an osteoinductive material comprising demineralized bone matrix, non-decalcified bone matrix, with or without hyaluronic acid;

(c) a scaffolding material selected from the group consisting of cancellous bone, chitosan, chitosan-protein, and chitin-protein fibers; and

(d) a gel material selected from the group consisting of chitosan, imidazolyl chitosan, methylpyrrolidinone chitosan, carbodiimide chitosan, glutaraldehyde chitosan, and a mixture of alginate with chitosan or a chitosan derivative.

4. The composition of claim 1, wherein one or more of the said materials is basic fibroblast growth factor, a vascular endothelial growth factor, platelet derived endothelial growth factor, bone, or supernatant fluid from a culture of cells known to produce angiogenic factors; another material of said composition is a mixture of demineralized bone matrix and non-decalcified bone matrix; the scaffolding material is cancellous bone; and the gel material is selected from the group

Express Mail No. EL 739387695 US

JMA 2977

PATENT

consisting of chitosan, alginate, hyaluronic acid, a mixture of
10 chitosan and alginate, or a mixture of hyaluronic acid and
chitosan.

5. The composition of claim 4, wherein one or more of the
said materials is basic fibroblast growth factor, platelet
derived endothelial growth factor, or vascular endothelial
growth factor and is present at 10^{-6} to 30 mg/ml; the
5 demineralized bone matrix is present at 5-30%; the non-
decalcified bone matrix is present at 5-30%; the scaffolding
material is cancellous bone milled to 0.1-1.5mm in its longest
diameter and is present at 10-40%; and the gel material is a
0.5-5% (w/v) concentration selected from the group consisting
10 of chitosan, alginate, hyaluronic acid, a mixture of alginate
with chitosan, present at 10-80%, or a mixture of hyaluronic
acid and chitosan.

6. The composition of claim 4, wherein one or more of the
said materials is an effective amount of fibroblast growth
factors or vascular endothelial growth factors; the
demineralized bone matrix is present at 10%; the cancellous
5 bone is present at 10%; and the gel material is a 3% (w/v)
concentration of alginate, or a mixture of alginate with
chitosan.

7. A composition of claim 6, wherein said fibroblast
growth factor is present at <1 mg/ml.

Express Mail No. EL 739387695 US
JMA 2977
PATENT

8. A composition of claim 6, wherein said vascular endothelial growth factors are present at <1 mg/ml.

9. The composition of claim 4, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 20%; the cancellous bone is present at 20%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

10. A composition of claim 9, wherein said fibroblast growth factor is present at <1 mg/ml.

11. A composition of claim 9, wherein said vascular endothelial growth factors are present at <1 mg/ml.

12. The composition of claim 4, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10%; the cancellous bone is present at 30%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

13. A composition of claim 12, wherein said fibroblast growth factor is present at <1 mg/ml.

Express Mail No. EL 739387695 US
JMA 2977
PATENT

14. A composition of claim 12, wherein said vascular endothelial growth factors are present at <1 mg/ml.

15. The composition of claim 4, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10-15% (w/w); the cancellous bone is present at 15-25% (w/w); and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

16. A composition of claim 15, wherein said fibroblast growth factor is present at <1 mg/ml.

17. A composition of claim 15, wherein said vascular endothelial growth factors are present at <1 mg/ml.

18. The composition of claim 2, wherein one or more of the angiogenesis-stimulating materials is basic fibroblast growth factor, a vascular endothelial growth factor, platelet derived endothelial growth factor, bone, or supernatant fluid from a culture of cells known to produce angiogenic factors; the osteoinductive material of said composition is a mixture of demineralized bone matrix and non-decalcified bone matrix; the scaffolding material is cancellous bone; and the gel material is selected from the group consisting of alginate, chitosan,

Express Mail No. EL 739387695 US

JMA 2977

PATENT

10 hyaluronic acid, a mixture of chitosan and alginate, or a
mixture of hyaluronic acid and chitosan.

19. The composition of claim 18, wherein one or more of
the said angiogenesis-stimulating materials is basic fibroblast
growth factor, platelet derived endothelial growth factor, or
vascular endothelial growth factor and is present at 10^{-6} to 30
5 mg/ml; the demineralized bone matrix is present at 5-15%; the
non-decalcified bone matrix is present at 5-15%; the
scaffolding material is cancellous bone milled to 0.1-1.5mm in
its longest diameter and is present at 10-40%; and the gel
material is a 2-5% (w/v) concentration selected from the group
10 consisting of chitosan, alginate, hyaluronic acid, a mixture of
alginate with chitosan, present at 35-80%, or a mixture of
hyaluronic acid and chitosan, present at 35-80%.

20. The composition of claim 18, wherein one or more of
the said materials is an effective amount of fibroblast growth
factors or vascular endothelial growth factors; the
demineralized bone matrix is present at 10%; the cancellous
5 bone is present at 10%; and the gel material is a 3% (w/v)
concentration of alginate, or a mixture of alginate with
chitosan.

21. A composition of claim 20, wherein said fibroblast
growth factor is present at <1 mg/ml.

22. A composition of claim 20, wherein said vascular

Express Mail No. EL 739387695 US
JMA 2977
PATENT

endothelial growth factors are present at <1 mg/ml.

23. The composition of claim 18, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 20%; the cancellous bone is present at 20%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

24. A composition of claim 23, wherein said fibroblast growth factor is present at <1 mg/ml.

25. A composition of claim 23, wherein said vascular endothelial growth factors are present at <1 mg/ml.

26. The composition of claim 18, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10%; the cancellous bone is present at 30%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

27. A composition of claim 26, wherein said fibroblast growth factor is present at <1 mg/ml.

28. A composition of claim 26, wherein said vascular

Express Mail No. EL 739387695 US
JMA 2977
PATENT

endothelial growth factors are present at <1 mg/ml.

29. The composition of claim 18, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10-15% (w/w); the cancellous bone is present at 15-25% (w/w); and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

30. A composition of claim 29, wherein said fibroblast growth factor is present at <1 mg/ml.

31. A composition of claim 29, wherein said vascular endothelial growth factors are present at <1 mg/ml.

32. The composition of claim 3, wherein one or more of the angiogenesis-stimulating materials is basic fibroblast growth factor, a vascular endothelial growth factor, platelet derived endothelial growth factor, bone, or supernatant fluid from a culture of cells known to produce angiogenic factors; the osteoinductive material of said composition is a mixture of demineralized bone matrix and non-decalcified bone matrix; the scaffolding material is cancellous bone; and the gel material is selected from the group consisting of alginate, chitosan, or a mixture of chitosan and alginate.

Express Mail No. EL 739387695 US

JMA 2977

PATENT

33. The composition of claim 32, wherein one or more of the said angiogenesis-stimulating materials is basic fibroblast growth factor, platelet derived endothelial growth factor, or vascular endothelial growth factor and is present at 10^{-6} to 30 mg/ml; the demineralized bone matrix is present at 5-15%; the non-decalcified bone matrix is present at 5-15%; the scaffolding material is cancellous bone milled to 0.1-1.5mm in its longest diameter and is present at 10-40%; and the gel material is a 2-5% (w/v) concentration selected from the group consisting of chitosan, alginate, or a mixture of alginate with chitosan, present at 35-80%.

34. The composition of claim 32, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10%; the cancellous bone is present at 10%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

35. A composition of claim 34, wherein said fibroblast growth factor is present at <1 mg/ml.

36. A composition of claim 34, wherein said vascular endothelial growth factors are present at <1 mg/ml.

37. The composition of claim 32, wherein one or more of the said materials is an effective amount of fibroblast growth

Express Mail No. EL 739387695 US
JMA 2977
PATENT

factors or vascular endothelial growth factors; the demineralized bone matrix is present at 20%; the cancellous bone is present at 20%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

38. A composition of claim 37, wherein said fibroblast growth factor is present at <1 mg/ml.

39. A composition of claim 37, wherein said vascular endothelial growth factors are present at <1 mg/ml.

40. The composition of claim 32, wherein one or more of the said materials is an effective amount of fibroblast growth factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10%; the cancellous bone is present at 30%; and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

41. A composition of claim 40, wherein said fibroblast growth factor is present at <1 mg/ml.

42. A composition of claim 40, wherein said vascular endothelial growth factors are present at <1 mg/ml.

43. The composition of claim 32, wherein one or more of the said materials is an effective amount of fibroblast growth

Express Mail No. EL 739387695 US
JMA 2977
PATENT

factors or vascular endothelial growth factors; the demineralized bone matrix is present at 10-15% (w/w); the cancellous bone is present at 15-25% (w/w); and the gel material is a 3% (w/v) concentration of alginate, or a mixture of alginate with chitosan.

44. A composition of claim 43, wherein said fibroblast growth factor is present at <1 mg/ml.

45. A composition of claim 43, wherein said vascular endothelial growth factors are present at <1 mg/ml.

46. A composition for promoting the growth and strengthening of bone comprising a mixture of a chitosan or chitosan derivative, cancellous bone, and demineralized bone matrix.

47. A composition of claim 46, wherein said composition comprises demineralized bone matrix is present at 10%; the cancellous bone is present at 10%; and the gel material is a 3% (w/v) of chitosan or chitosan derivative.

48. A composition of claim 46, wherein said composition comprises demineralized bone matrix is present at 20%; the cancellous bone is present at 20%; and the gel material is a 3% (w/v) of chitosan or chitosan derivative.

49. A composition of claim 46, wherein said composition

Express Mail No. EL 739387695 US
JMA 2977
PATENT

comprises demineralized bone matrix is present at 10%; the cancellous bone is present at 30%; and the gel material is a 3% (w/v) of chitosan or chitosan derivative.

50. A composition for promoting the growth and strengthening of bone comprising a mixture of alginate, calcium, cancellous bone, and demineralized bone matrix.

51. A composition of claim 50, wherein said composition comprises demineralized bone matrix is present at 10%; the cancellous bone is present at 30%; and the gel material is a 3% (w/v) of alginate with or without calcium.

52. A composition of claim 50, wherein said composition comprises demineralized bone matrix is present at 20%; the cancellous bone is present at 20%; and the gel material is a 3% (w/v) of alginate with or without calcium.

53. A composition of claim 50, wherein said composition comprises demineralized bone matrix is present at 10%; the cancellous bone is present at 10%; and the gel material is a 3% (w/v) of alginate with or without calcium.

54. A composition for promoting the growth and strengthening of bone comprising a mixture of chitosan or chitosan derivative, alginate, cancellous bone, and demineralized bone matrix.

Express Mail No. EL 739387695 US
JMA 2977
PATENT

55. A composition of claim 54, wherein said composition comprises demineralized bone matrix is present at 20% (w/w); the cancellous bone is present at 12% (w/w); and the gel material is 0.5% (w/w) alginate, 0.3% (w/w) chitosan.

56. A composition for promoting the growth and strengthening of bone comprising a mixture of hyaluronic acid, cancellous bone, and demineralized bone matrix.

57. A method of inducing bone formation in a vertebrate comprising applying a composition selected from the group consisting of the compositions of claims 1-56 to a site in the vertebrate where bone formation is desired.

58. The method of claim 57, wherein the site is the junction of an allograft or autograft and a bone.

59. The method of claim 57, wherein the site is the junction of a bone and a bone prosthesis.

60. The method of claim 57, wherein the site is a fracture.

61. A method of filling a bone defect comprising filling the bone defect with a rigid material consisting essentially of chitin or chitosan.

62. The method of claim 61, wherein the bone defect is a

63. The method of claim 61, wherein the bone defect is a spinal disc and the rigid material is a spinal prosthesis.

64. The method of claim 61, wherein the rigid material comprises chitin or chitosan cross-linked with glutaraldehyde, carbodiimide, lysine, or vinyl.